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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,633	06/28/2001	Timothy W. Conner	38-21(15856)B	9354

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/894,633	CONNER ET AL.	
	Examin r	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communicati n appears on the cov r sh t with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *13-17,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, SEQ ID NO: 81 in the paper filed October 6, 2003 is acknowledged. The traversal is on the ground(s) that there is no burden on examination. With regard to Applicant's argument for rejoinder of Groups I and II, this argument is found persuasive. Therefore, claims 1-12 and 18, representing the claims of both Groups I and II will be examined with respect to SEQ ID NO: 81. However, Applicant's argument is not found persuasive with regard to the other groups because each of the other groups requires different prior art searches to meet the additional limitations of the groups, are classified separately and may have different enablement and description issues. Therefore, there would be a burden in the examination of these additional groups.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-12 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of plant nucleic acids which are different from those disclosed in the specification. The genus includes a number of variants for which no written description is provided in the specification, due to the language which permits sequences comprising fragments, regions or cis elements. This large genus is represented in the specification by only the particularly named SEQ ID No: 81. Thus, applicant has express possession of only one sequence, SEQ ID NO: 81, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitation of being capable of regulating transcription is provided.

Further, these claims encompass allelic variants of the promoter fragments including insertions and mutations and further upstream and downstream sequences.

No written description of alleles or of upstream or downstream regions containing additional sequence.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the fragments, cis elements and regions of SEQ ID NO: 81 lack any specific structure since a single nucleotide is a fragment of SEQ ID NO: 81. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the SEQ ID NO: 81, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "fragments, regions or cis elements", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred,

> that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a promoter, without any definition of the particular sequences necessary for promoter function.

In the instant application, SEQ ID NO: 81 is described. In Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID NO: 81. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-12 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 81, does not reasonably provide enablement for fragments, cis elements or regions of SEQ ID NO: 81 as promoter

elements. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a nucleic acid comprising SEQ ID NO: 81 and fragments, cis elements, regions and transgenic plants thereof. The invention is in an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass any sequence with any fragment of SEQ ID NO: 81. This breadth includes, since SEQ ID NO: 81 has all four nucleotide bases, A, C, G, and T, any sequence which has an A, a G, a C or a T, therefore essentially comprising any nucleic acid whatsoever that meets the functional requirement of having promoter

activity. The method of making the transgenic plant essentially comprises making any transgenic plant due to the breadth of the fragment language.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the ability of sequences to function as promoters and there is significant variation in the tissue expression and functional activity of promoters. Screening fragments of SEQ ID NO: 81 to determine which fragments comprise promoter sequences is an inventive, unpredictable and difficult undertaking in itself, and the efficacy of the promoter will vary in different plants, in different tissues and in different cell types. Claims 1-12 and 18 permit expression in any transgenic plant but it is entirely unpredictable whether the full length sequence would have promoter activity in other plants, much less fragments, cis elements or regions of SEQ ID NO: 81. This would require inventive effort, with many intervening steps, to achieve effective reduction to practice, with there being no guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The prior art teaches that promoter activity, particularly in plants, is significantly unpredictable. In particular, the specific sequences are critical and one cannot simply randomly select fragments, cis elements or regions and expect these subfragments to have promoter activity. Even the art cited by Applicant in the IDS supports this notion. For example, Hamilton et al (Plant Mol. Biol. (1998) 38:663-669) states "The inability of the -420 to -90 CaMV 35S promoter to enhance the expression of the - 101 bp pollen promoter (Figure 1) indicates that the enhancer sequences in the 355 promoter are unable to enhance the activity of the pollen specificity domain (-84 to -53). Thus the 6

bp quantitative element in the ZM13 promoter appears to show a specificity for the pollen-expression element. It cannot be replaced by other quantitative elements such as those present in the 35S promoter that are known to function in other plant tissues." This is an express statement that promoter activity is specific and is limited to particular sequences. Hamilton shows that the result of modifying promoter sequences is unpredictable and in the specific case, modifications did not permit promoter function.

Zabaleta (Plant Journal (1998) 15(1):49-59) supports the notion that identification of active regions, even in anther specific promoters, is unpredictable, noting that "Common cis-elements might exist but their functional similarity may be less obvious at the sequence level. As an example, it has been shown that the OPAQUE2 transcription factor binds to completely different sequences in two different gene promoters (see page 57, column 2)." Thus, in the absence of a definition of subregions of promoter function by the specification, it is unpredictable based solely on sequence information what cis elements and subregions are functional as the promoter elements.

Nilsson (Plant Mol. Biol. (1996) 31:887-895) teaches "Our results demonstrate that the activities of rolC and 35S promoters varied in very different, unpredictable ways during the annual cycle of growth and dormancy (see abstract)". This result shows that the specificity and activity, even of well known plant promoters such as CaMV 35S, are unpredictable during growth.

Finally, it is entirely unpredictable which fragments of SEQ ID NO: 81 will function as promoters. Further, it is entirely unpredictable what activity, if any, fragments of the sequence would have.

Working Examples

The specification has a working example of SEQ ID NO: 81 as a functional promoter in wheat (see page 80, table, for example).

Guidance in the Specification.

The specification itself supports the unpredictability of promoter function in general, and in plants in particular. At page 80 of the specification, the table shows that the Applicant has tested at least 26 different sequences for promoter activity. In this sample of putative promoters, 12, or nearly half, had no promoter activity at all. Of the remaining 14 putative promoters, 8 had low activity according to the specification and only 6 had medium level promoting activity. None had high level promoter activity. So the guidance in the specification is that it is unpredictable whether sequences, clearly expected to be possible promoters based on Applicant's decision to test them for promoter activity, actually have promoter activity. At page 82 of the specification, the specification notes that activity in a broad spectrum of plants may be indicated by expression in arabidopsis. Failure of activity is impliedly showing that there is not a broad spectrum of plants in which the promoter is active based on page 82. For SEQ ID NO: 81, the table at page 83 shows no evidence that this nucleic acid has promoter activity in a wide variety of plants, but is only shown to function in wheat. In fact, at page 84, the specification shows that SEQ ID NO: 81 has a very restricted expression pattern and is anther specific.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability shown in the prior art and in the specification mitigate against enablement for fragments of SEQ ID NO: 81. The specification teaches the unpredictability of promoter function, even in a series of expected promoters, 12 did not function. One of skill in the art cannot readily anticipate the effect of a truncation of SEQ ID NO: 81 and one cannot envision what regions of SEQ ID NO: 81 will have promoter activity. Further the specification does not provide guidance to overcome art recognized problems in the use of fragments of SEQ ID NO: 81 as promoters as broadly claimed. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of fragments of SEQ ID NO: 81 and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Interpretation

6. As noted above in the description rejection, the claims are open to any nucleic acid which comprises a fragment of SEQ ID NO: 81, so long as the nucleic acid is capable of promoter activity. Thus, even a single base from SEQ ID NO: 81 is a fragment of that sequence, and a sequence which comprises such a single base, and which has promoter activity, would render claim 1 anticipated. The specification, at page 27, clearly permits such a reading, stating that a fragment is any piece less than full length. The largest specific fragment length given is 30 nucleotides, with lengths of

8, 15 and 20 being specifically mentioned. The rejections below rely upon the fragment, cis element and region language. Further, because the claims are drawn to any fragment, and the patent office lacks any way to assess whether a particular fragment has promoter activity, the sequence will be relied upon as anticipatory. As MPEP 2112.01 notes ""Products of identical chemical composition can not have mutually exclusive properties." As MPEP 2111 notes "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." Currently, there is no evidence of record showing which regions of SEQ ID NO: 81 have promoter activity and which regions do not.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 5, 8 and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AP001526 (May 30, 2000).

Genbank Accession No. AP001526 teaches a nucleic acid which comprises 30 nucleotides of SEQ ID NO: 81 (see alignment).

With regard to claim 2, the sequence is a fragment of SEQ ID NO: 81, which the specification states is a promoter sequence.

With regard to claims 3 and 5, the clone has the T7 and SP6 promoters as well, making the sequence a hybrid promoter and providing a minimal promoter sequence (see alignment).

With regard to claim 11, this sequence was in a clone, RP11-727C13, which is grown in E. coli, which sequence annotation shows transcribable sequence and 3' non translated sequence (see alignment).

9. Claims 1-12 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Zabaleta et al (Plant J. (1998) 15(1):49-59).

Zabaleta teaches, with regard to claims 1 and 8, a nucleic acid which comprises a sequence which comprises ACCCACA (see sequence in bold, page 52, figure 2, panel A, in –190 nucleotide line) which is 100% identical to the ACCCACA at positions 346-352 of SEQ ID NO: 81.

With regard to claims 2, 4, 9 and 10, Zabaleta teaches that the sequence which comprises ACCCACA is an anther specific promoter (see page 53, column 1 to column 2, where the –218/-112 region of the 55kDa protein was shown to have anther specific activity).

With regard to claims 3 and 5-7, Zabaleta teaches that the sequence was fused to a CaMV 35S promoter (see page 53, column 1).

With regard to claims 11 and 12, Zabaleta teaches a transgenic arabidopsis plant which comprises the sequence ACCCACA in its context operably linked to the CaMV 35S promoter, to the transcribable GUS enzyme, with a 3' non-translated plasmid region (see page 53, columns 1 and 2).

With regard to claim 18, Zabaleta teaches making a transgenic plant comprising introducing the promoter sequence comprising ACCCACA operably linked to GUS and a 3' nontranslated region into the cell of a plant (see page 53 and page 58, column 2, subheading "plant transformations").

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman

JEFFREY FREDMAN
PRIMARY EXAMINER